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10/680,635	10/07/2003	Hans-Georg Ihlenfeldt	BMID9967CUS	5091

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EXAMINER	
KIM, ALEXANDER D	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	**Application No.** 10/680,635	**Applicant(s)** IHLENFELDT ET AL.	
	Examiner Alexander D. Kim	**Art Unit** 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 20 September 2006.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 15-26 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 15-26 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 07 October 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/416,579.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 04/09/2004.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. By virtue of a preliminary amendment filed on 09/20/2006, claims 1-14 has been canceled; and claims 15-26 has been added. Thus, claims 15-26 are pending in this instant case.

Priority

2. Applicant's claim for the benefit of a continuation application of prior application 09/416579 filed on 10/12/1999 (now abandoned) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

The foreign patent applications 198 46 838.5 (filed in Germany on 12 October 1998) and 199 14 644.6 (filed in Germany on 31 March 1999) are provided in the parent application No. 09/416,579. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Said foreign priority document is not in English and no translation has been received.

Information Disclosure Statement

3. The information disclosure statement (IDS) filed on 04/09/2004 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Objections to the Specification

4. The specification is objected to because of the following informalities:

a. The specification is objected to because the title is not descriptive of the elected claims. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The examiner suggests the following new title, for example:

---A recombinant kinase from insect cells for the synthesis of nucleoside monophosphate---

b. The Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the name of the enzyme (deoxynucleoside kinase) for completeness.

c. In page 1, the ribose sugar ring is drawn as if there is four methyl substitution instead of hydrogen. Appropriate clarification is required.

d. The citation disclosed in p. 9 line 8, the author name is omitted in (b). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15-26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to a recombinant kinase accepting all natural deoxynucleosides as a substrate and derived from cells of a nonvertebrate organism.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

The instant specification teach a recombinant Drosophila melanogaster kinase (Dm-dNK) cloned into an E. coli strain BL21 for expression which has characteristics of using all natural deoxynucleosides as a substrate. However, the breadth of claim includes any nonvertebrate kinase which uses all natural deoxynucleosides as a substrate. The prior art teaches a species of kinase which accepts all four natural deoxynucleoside by Munch-Petersen from the same source, D. melanogaster. Thus the prior art and the instant specification do not describe any other nonvertebrate kinase able to use all natural deoxynucleoside and the structure of genus cannot be sufficiently described by the instant species. The kinase of instant specification and prior art do not describe a genus sufficiently to represent the correlation between the structure and function of claimed genus that is any kinase which uses all natural deoxynucleoside as substrate. Thus the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus of the instant specification.

6. Claims 15-26 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for Dm-dNK, does not reasonably provide enablement for any kinase accepting all natural deoxynucleosides as a substrate from any nonvertebrate organism. The specification does not enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to a recombinant kinase accepting all natural deoxynucleosides as a substrate and derived from cells of D. melanogaster. However, The breadth of claims includes any recombinant kinase accepting all natural deoxynucleosides as a substrate and derived from any nonvertebrate organism.

Applicants teach the Dm-dNK, however, applicants and prior art disclose no direction or guidance on how to make and use any other kinase which uses all natural deoxynucleoside as substrate. Thus the specification and prior art fail to describe how to make and use the claimed genus sufficiently. Therefore, it is unpredictable for preparing any kinase which uses all natural deoxynucleosides as substrate from any nonvertebrate organisms. For all of the above reason, it would require undue experimentation necessary for an instant genus kinase.

Claim Rejections - 35 USC § 102

> The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
>
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 15-26 are rejected under 35 U.S.C. 102(b) as being anticipated by reference by Munch-Petersen et al. (1998, February 13, The Journal of biological Chemistry, Vol. 273, p. 3926-3931) and evidenced by Johansson et al. (1999, August 20, The Journal of biological Chemistry, Vol. 274, p. 23814-23819).

Claims 15 (claims 16-21 dependent therefrom) and 22 (claims 23-26 dependent therefrom) are drawn to a recombinant kinase accepting all natural deoxynucleosides, from cells of nonvertebrate organism with additional limitations disclosed in claims 16-21 and 23-26.

Munch-Petersen et al. (Microbiology) teach a deoxynucleoside kinase isolated from "the D. melanogaster S-2 cell line of embryonic origin" (Dm-dNK) (see middle of left column, p. 3927). Because the term recombinant is not defined by the instant application and with the broadest reasonable interpretation, the kinase of Munch-Petersen et al. is considered a recombinant cell having a deoxynucleoside kinase gene from *D. melanogaster* thus producing a recombinant kinase. The deoxynucleoside kinase of Munch-Petersen et al. have "all four deoxynucleoside kinase activities" (see bottom right column, p. 3927) which makes up a DNA and the kinetic parameters are shown in Table III, p. 3929. The kinase of Munch-Petersen et al. has inherent stability during the catalytic reaction in the absence of a stabilizing SH reagent and a protein as evidenced by Johansson et al. who disclosing a recombinant Dm-dNK is fully active in the assay condition without SH reagent and a stabilizing proteins (see Johansson et al., middle of left column, p. 23815). Thus the deoxynucleoside kinase of Munch-Petersen et al. meets all the limitations of claims 15-16 and 21-22. The deoxynucleoside kinase of Munch-Petersen et al. has more than 20 units/mg (1 unit = 1 umol/min) and more than 10000 $M^{-1}s^{-1}$ for all four deoxynucleoside as shown in Table III (p. 3929) thus meets the limitations of claims 17-18 and 23-24. Because the instant kinase is comprised of the exact same amino acid sequence compared to Dm-dNK of Munch-Petersen et al., both kinase would have all inherent physical characteristic of D. melanogaster deoxynucleoside kinase. The kinase of Munch-Peterson et al. would have a half-life of more than equal to 50 hours at 37°C in Tris buffer with 5 mM $MgCl_2$, half-life of more than equal to 25 hours in water, and stable up to 60°C as disclosed by the instant specification page 3, lines 21-25, thus meets the limitations of claims 19-20 and 25-26. The kinase of Munch-Petersen et al. meets all limitations of claims 15-26.

8. Claims 15-26 are rejected under 35 U.S.C. 102(a) as being anticipated by reference by Johansson et al. (1999, August 20, The Journal of biological Chemistry, Vol. 274, p. 23814-23819).

Claims 15 (claims 16-21 dependent therefrom) and 22 (claims 23-26 dependent therefrom) are drawn to a recombinant kinase accepting all natural deoxynucleosides, from cells of nonvertebrate organism with additional limitations disclosed in claims 16-21 and 23-26.

Johansson et al. (Microbiology) teach an Dm-dNK expressed in "E. coli. strain BL21(DE3)pLysS" transformed with expression vector "pGEX-5X-1" with Dm-dNK gene derived from a D. melanogaster cDNA clone (see Cloning of Dm-dNK cDNA in Experimental Procedures in left column, p. 23815). Johansson et al. teach that "the enzyme phosphorylated the pyrimidine nucleosides dThd, dUrd, and dCyd as well as the purine nucleosides dAdo and dGuo (data not shown)" (see top right column, pl 23815) in the assay condition without SH reagents or any other stabilizing proteins (see middle of left column, p. 23815). Thus the DM-dNK of Johansson et al. meets all the limitations of claims 15-16 and 21-22. The DM-dNK of Johansson et al. has more than 20 units/mg (1 unit = 1 umol/min) and more than 10000 $M^{-1}s^{-1}$ for all four deoxynucleoside as shown in Table I (p. 3929, after conversion to units according to instant claims) thus meets the limitations of claims 17-18 and 23-24. Because the kinase of Johansson et al. is the kinase from exact same source having same amino acid sequence as the instant application, it would has a half-life of more than equal to 50 hours at 37°C in Tris buffer with 5 mM $MgCl_2$, half-life of more than equal to 25 hours in water, and stable up to 60°C as disclosed by the instant specification page 3, lines 21-25, thus meets the limitations of claims 19-20 and 25-26. The kinase of Munch-Petersen et al. meets all limitations of claims 15-26. This rejection can be overcome by providing a certified English translation of German application 198 46 838.5 (filed on 10/12/1998) and indicating supports for instant claim limitations from this priority document.

Claim Rejections - 35 USC § 102/103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 15-26 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Munch-Petersen et al. (1998, February 13, The Journal of biological Chemistry, Vol. 273, p. 3926-3931) and

Johansson et al. (1999, August 20, The Journal of biological Chemistry, Vol. 274, p. 23814-23819). Claims 15-21 are construed as product-by-process claims.

The factors to be considered for a product-by-process are summarized in MPEP 2113. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." See In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983) and Ex parte Gray, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989)

It would have been obvious to one of ordinary skill in the art to produce this protein by recombinant method because a recombinant method provide increased production thus advantageous for purification and more cost effective. Therefore, it would have been obvious to one of ordinary skill in the art to isolate and clone Dm-dNK gene into a host cell with an expression vector

The kinase of instant application appears to be identical to the kinase of Munch-Petersen et al. (1998). Therefore, it would have been obvious to produce instant kinase by recombinant expression of the kinase with a reasonable expectation of success because a recombinant method provide increased production of protein thus advantageous for purification and cost effective. The motivation to do so is provided by Johansson et al. who teach the usefulness of kinase which catalyze the rate-limiting step in the pharmacological activation of many nucleoside analogs (see Johansson et al., middle of left column, p. 23814). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander D. Kim whose telephone number is (571) 272-5266. The examiner can normally be reached on 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alexander Kim
September 21, 2006

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SUPERVISORY PATENT EXAMINER